UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,342	04/30/2001	George Jackowski	2132.026	3141

21917 7590 03/02/2004

MCHALE & SLAVIN, P.A.
2855 PGA BLVD
PALM BEACH GARDENS, FL 33410

EXAMINER	
NGUYEN, BAO THUY L	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/02/2004

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,342	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 36-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 36-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed July 31, 2003 has been received. Claims 2-35 have been canceled. Claims 36-43 have been added. Claims 1 and 36-43 are pending.

2. All rejections not reiterated herein below are withdrawn in view of the amendment and/or cancellation of the claims.

3. The text of those US codes not found in this office action may be found in a previous office action.

Specification

4. The amendment filed July 31, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the alteration of SEQ ID NO. 1 is improper. Therefore, the changes to Figures 1 and 2 are improper.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. The claimed invention is directed to non-statutory subject matter. Claim 1 reads on a naturally occurring protein. It is suggested that applicant inserts either -isolated— or -synthetic--, if the protein is synthetic, between "a" and "biopolymer" for clarity.

Claim Rejections - 35 USC § 112, second paragraph

7. Claims 36-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36-40 are vague and indefinite with respect to the recitation in step c. It is unclear what criteria are used in comparing the mass spectrum profile of the detected sample to the mass spectrum profile of a peptide having amino acid residues 2-12 of SEQ ID NO. 1 (herein after SEQ ID No. 1 (2-12)) . Does this mean a 100% match? Is it the same to say that detection of SEQ ID NO. 1 (2-12) in the patient sample is diagnostic for myocardial infarction? If so, it is suggested that applicant amends the claims such as to clearly and concisely claim the invention.

The claims are also confusing because it is unclear what characteristics are used as the basis of comparison. These "characteristics" have not been clearly defined.

Claim Rejections - 35 USC § 112, first paragraph

8. Claims 1 and 36-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

SEQ ID No. 1 has been amended such that it does not find support in the specification as originally filed. A preliminary amendment filed on April 23, 2002 deleted the amino acid listing (GDFLAEGGGVR) in the specification and replaced it with SEQ ID NO. 1, identified as a peptide having a molecular weight of about 1077 daltons. A CRF for SEQ ID No. 1 dated

5/9/02 was submitted identifying SEQ ID NO. 1 as a biopolymer marker having 11 amino acids (GDFLAEGGGVR). Subsequently, a new sequence listing was submitted (dated 8/11/03) modifying SEQ ID NO. 1 by adding 2 more amino acid residues with the first and last residues in parentheses indicating predicted amino acids. Therefore, SEQ ID NO. 1 is currently a peptide having 13 amino acids; this is an improper addition of material to the specification. The invention, as amended, is different from what is defined in the claim(s) and the originally specification because nothing in the specification leads one to predict that the peptide comprises 13 amino acids with the first and last being Glu and Gly respectively.

Applicant is required to cancel the new matter in response to this final action.

9. Claims 36-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claims 36-40 recite a method for diagnosing myocardial infarction by detecting a biopolymer marker from a patient sample and comparing the detected biopolymer marker to the biopolymer marker having SEQ ID NO. 1 (2-12). Recognition of a mass spectrum profile in the detected sample displaying the characteristic profile of the mass spectrum profile of SEQ ID No. 1 (2-12) is diagnostic for myocardial infarction. Such a method is not supported by the specification as originally filed. The specification at pages 26-31 discloses how a biopolymer marker identified as SEQ ID NO. 1 was identified from patient serum samples, however, nowhere in the specification is there is teaching of detecting any other biopolymer marker, comparing the detected marker to SEQ ID NO. 1 (2-12), and determining a disease state

from the detected marker. Furthermore, it is unclear what criteria are used in comparing the mass spectrum profile of the detected sample to the mass spectrum profile of SEQ ID NO. 1 (2-12). The claim recites that recognition of a mass spectrum profile in the sample displaying the characteristic profile of mass spectrum profile for the peptide consisting of SEQ ID NO. 1 (2-12) is diagnostic for MI; however, there is no clear teaching of this in the specification or anywhere else. Applicant is required to cancel the new matter.

10. Claims 36-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Claims 36-40 are directed to a method for diagnosing myocardial infarction by detecting at least one biopolymer marker from a patient sample and comparing the detected biopolymer to SEQ ID NO. 1 (2-12). Recognition of a mass spectrum profile in the sample displaying the characteristic profile of the mass spectrum profile for SEQ ID NO. 1 (2-12) is diagnostic for myocardial infarction. Such a method has not been describe in the specification in such a way as to enable one skill in the art to make and use the invention as claimed.

The specification states that a biopolymer marker having SEQ ID NO. 1 was found in serum samples of patients suffering from a variety of disease states (specification, page 26, lines 20-22) including MI, (specification, page 27, lines 17-23.) However, the specification does not have any data supporting this assertion. Data presented in Figure 1 and in the declaration dated July 31, 2003 is not convincing, nor does it clearly demonstrate that SEQ ID NO. 1 is indicative of MI. The specification at page 26, line 20 teaches that serum samples from patients suffering from a variety of diseases were analyzed using protein chips and the profiles were analyzed to discern notable sequences that were deemed in some way evidentiary of at least one disease state. The specification goes on to say that the samples were concentrated by centrifugation and the filtrate was discarded and the retained solution, containing the two peptides of interest, was analyzed by tandem mass spectrometry. As a result of these procedures the disease specific marker consisting of SEQ ID NO. 1 was found. The specification asserts that from data set forth in Figure 1, this marker is indicative of MI.

It is unclear how SEQ ID NO. 1 was identified as a "notable sequence" or how it was deemed "evidentiary" of a disease state. There is nothing specific in the procedure that would enable one to choose SEQ ID NO. 1 as a notable sequence among all other possible proteins or peptides present in a sample. There is no nexus between the procedure for screening samples from patients suspected of having a variety of different diseases, identifying SEQ ID NO. 1 as a disease marker, and determining that SEQ ID NO. 1 is diagnostic for MI.

According to Strongin (1993, "Sensitivity, Specificity, and Predictive Value of Diagnostic Tests: Definitions and Clinical Applications", in Laboratory Diagnosis of Viral Infections, Lennette, e., ed., Marcel Dekker, Inc., New York, pp. 211-219) a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics

include the following: (1) the sensitivity of the assay; (2) the true-positive test rate; (3) the false-negative test rate; (4) the specificity, or percentage of patients without the disease who will display a negative results; (5) the true-negative test rate; (6) the false-positive test rate; (7) the predictive value, or the probability that the test result is correctly indicating the presence or absence of the disease; (8) the prevalence, or number of patients in any given population that have the disease in question; (9) the efficiency or percentage of all results that are true; (10) the accuracy of the recited diagnostic assay. Additional considerations must also be examined to enable the clinician to practice the invention including assessment of the following: (1) when is the maximum sensitivity desired?; (2) when is the maximum specificity desired?; (3) when is the maximum efficiency desired?; (4) How is the maximum sensitivity or specificity achieved?; (5) how is the predictive value maximized? An essential understanding of these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test. Since the specification lacks any teaching of how the diagnostic tests were performed, or any information regarding the patients from which the samples were taken, and whether any considerations were given to any of the characteristics state above, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

The specification lacks proper guidance to enable one skill in the art to determine the incidence of disease as related to the presence or absence of a biopolymer that correspond to the maker having SEQ ID NO. 1 (2-12). The specification further lack proper guidance to enable one skilled in the art to distinguish between any and all disease states as claimed.

Because of the lack of description in the specification for the claimed method, it cannot be conclusively determined from the data presented in Figure 1 nor the declaration that anyone or everyone who has this polypeptide marker suffers from any diseases, specifically MI. Patent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001. That requirement has not been met in this specification with respect to a method for diagnosing MI by detecting a biopolymer marker in a patient sample and comparing the detected biopolymer to a biopolymer marker having SEQ ID. NO. 1 (2-12).

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

11. Applicant's arguments filed July 31, 2003 have been fully considered but they are not persuasive.

Applicant argues that the claims, as amended, find clear support in the specification because claims 36 is now drawn to a method for diagnosing MI wherein the mass spectrometric profile of peptides elucidated from patient samples are compared with the mass spectrometric profile of a peptide consisting of SEQ ID NO. 1 (2-12). If the profile of the peptide consisting of

SEQ ID NO. 1 (2-12) is identified within the sample profile it is concluded that the peptide consisting of SEQ ID NO. 1 (2-12) is found in the sample and such peptide is diagnostic for MI.

This argument is not persuasive. Claim 36 does not recites the detection, by mass spectrometric profile, of a peptide consisting of SEQ ID NO. 1 (2-12) in a patient sample. Claim 36 recites the detection, by mass spectrometric profile, of any discernible peptide fragments in a sample and comparing the detected peptide fragments to the mass spectrometric profile of SEQ ID NO. 1 (2-12). Claim 36 further recites that the recognition of a mass spectrum profile in the sample displaying the characteristics profile of SEQ ID NO. 1 (2-12) is diagnostic for MI. This method does not have support in the specification as originally filed, nor is it the same method as argued by Applicant. Furthermore, it is unclear what characteristics are used as a basis for comparison. These characteristics have not been positively identified. It is also unclear what manner would be considered "effective to maximize elucidation of discernible peptide fragments".

Applicant argues that the originally filed figures show that the peptide consisting of SEQ ID NO. 1 (2-12) was found in the serum of patients with a history of MI. Applicant also argues that the instant invention strive to specify particular markers which are evidentiary of at least one particular disease state, whereby the presence of said marker serves as a positive indicator of disease.

It is noted that these arguments are directed toward newly added claims which have not been considered up until now, however, these arguments have been considered with respect to the new claims and are not found to be persuasive. As stated above, there is no clear and convincing evidence that the presence of SEQ ID NO. 1 (2-12) is diagnostic for MI. The specification teaches the identification of SEQ ID NO. 1 (2-12) in serum samples from patients

suffering from a variety of disease states including those diseases associated with the complement system and Syndrome X (specification, page 12). The specification lacks any description of how SEQ ID NO. 1 (2-12) was determined to be evidentiary of a disease state or how it was specifically related to MI. The assertion that patients having a history of MI show a peptide consisting SEQ ID NO. 1 (2-12) in their serum is not convincing. Results from a total of 5 patients were submitted as evidentiary, however this is not statistically significant. Specifically, it is not clear how the diagnostic assay was designed and how the data was interpreted as discussed above. The specification does not have any teaching that can positively tie the peptide to a specific disease because the peptide was identified from samples of patients suffering from a variety of diseases (specification, page 12). Therefore, how is it that this peptide is determined to be diagnostic for MI?.

Applicant argues that the declaration shows a side-by-side profiles of normal sera and sera from a patients having a history of MI, and that this profile clearly evidences the absence of the 1077 dalton marker in normal sera and thus establishes the specificity of the 1077 dalton peptide as a marker diagnostic for MI.

This argument has been fully considered but is not deemed to be persuasive. A showing of one patient sample and one negative control does not lead to a generalization that the presence of such marker is diagnostic for MI, i.e. it does not necessarily show the specificity of the marker to a specific disease. Specifically, there is no consideration of the specificity, or percentage of patients without the disease who will display a negative result; nor is there a consideration of the sensitivity of the assay, the true-positive test rate, the false-negative test rate, the predictive value, or the probability that the rest result is correctly indicating the presence or absence of the disease, etc.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 9:00 - 4:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641

20 February 2004